CASE REPORT

A case report of venous thrombosis in a leprosy patient treated with corticosteroid and thalidomide

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Summary Thalidomide is the drug of choice in the treatment of severe erythema nodosum leprosum (ENL) in men. It has recently been associated with deep venous thrombosis (DVT) when used in treatment of refractory multiple myeloma along with combination chemotherapy. We report a case of DVT in a patient treated for ENL with corticosteroids and thalidomide, and suggest a possible mechanism for the association.

Introduction

Thalidomide is the drug of choice in the treatment of severe erythema nodosum leprosum (ENL) in men.1 The ever increasing spectrum of diseases for which thalidomide has been beneficial, brings to light its various hitherto unrecognised complications. Thalidomide has recently been associated with life-threatening deep venous thrombosis (DVT) when used in the treatment of refractory multiple myeloma along with combination chemotherapy.2,3 However, its occurrence in relation to use in the treatment of recalcitrant ENL has been reported only once in literature.4 Here we report a case of DVT in a patient treated for recalcitrant ENL treated with corticosteroid and thalidomide.

Case Report

A 35 year old male with lepromatous leprosy, in type 2 lepra reaction with recurrent erythema nodosum leprosum (ENL) of one year’s duration, presented with an acute episode of multiple erythematous tender nodules, myalgia, arthralgia, dactylitis and redness of the eyes. He had been on treatment with multibacillary multi drug therapy (MBMDT) and prednisolone (40–60 mg/day) for the previous 7 months. On examination, the patient had cushingoid...
habitus and multiple necrotic ENL lesions over the gluteal region and extremities. The prednisolone was increased to 60 mg/day, with clinical improvement. When the dose was tapered after 2 weeks, he developed new ENL lesions. Hence, thalidomide was added in the dose of 300 mg/day in divided doses. His ENL lesions started to abate by the fourth day. After a lesion free period of 2 weeks, thalidomide was tapered to 200 mg/day then 100 mg/day. After two more weeks he was maintained on 50 mg/day. Meanwhile, the steroid dose was tapered to 20 mg/day over the next 6 weeks and subsequently the patient was discharged from the hospital.

At follow-up 6 weeks after starting thalidomide, we noticed swelling of both the legs with fullness of the right popliteal fossa, posterior calf tenderness and warmth, and a negative Homan’s sign. Doppler ultrasonography revealed bilateral DVT of the popliteal veins with proximal extension. Blood investigations revealed neutrophilic leucocytosis and a normal coagulation profile. Thalidomide was stopped. Anticoagulation was initiated with low molecular weight heparin and maintained with warfarin. The swelling of the legs gradually subsided over 4 days and the patient was continued on warfarin for 6 months.

Discussion

In the last 12 years, we have managed about 10 cases of type 2 lepra reaction with thalidomide; DVT was not noted in any of them until this case. There have been very few reports of DVT in leprosy patients receiving thalidomide for ENL, so the association could be co-incidental. However there are reports of DVT in patients receiving thalidomide as part of their treatment for multiple myeloma, and there is a possible mechanism for thrombosis in patients receiving thalidomide together with corticosteroids.

Instances of DVT triggered by thalidomide have been reported in the induction phase of combination chemotherapy especially with doxorubicin and cyclophosphamide in patients with multiple myeloma and other malignancies. DVT has also been seen in patients with lupus erythematosus receiving low dose thalidomide. The presence of a hypercoagulable state, destruction of tumour cells or an intrinsic procoagulable state may predispose to thromboembolic events in patients with multiple myeloma. But there was no increased incidence of DVT when thalidomide was administered as a single agent, suggesting that other chemotherapeutic agents including cyclophosphamide and corticosteroids when coadministered with thalidomide, may precipitate venous thromboembolism. In our case no clinical risk factor for DVT could be identified, but for a relative immobility during reactional episodes.

In the case report of recurrent erythema nodosum leprosum by Sharma et al., their patient on thalidomide developed DVT after an initial pulse of dexamethasone cyclophosphamide. Thalidomide is a potent inhibitor of tumor necrosis factor alpha (TNF). That inhibition of TNF leads to decreased expression of thrombomodulin, which is an anticoagulant molecule. However, this effect on its own is insufficient to explain the thrombosis because thalidomide alone does not predispose to significant venous thrombosis even in hypercoagulability states. Since the active molecules involved in coagulation and anticoagulation are tissue specific, it may be hypothesised that the peripheral vasculature may be more sensitive to the anticoagulant effects of thrombomodulin. In addition, steroids bring about negative regulation of cytokine genes in endothelial cells, macrophages and lymphocytes, thereby decreasing the production of TNF-alpha and interleukin (IL)-1. This synergistic suppression
of expression of thrombomodulin, by a combined effect of thalidomide and steroids, might bring about thrombosis. In resource-poor settings, patients with refractory ENL lesions are usually on treatment with steroids before being started on thalidomide because of the high cost and difficulties of access to the drug. This may predispose them to risk of venous thromboembolism when thalidomide is added. DVT may be missed because oedema of the legs is a common occurrence during ENL in leprosy. This case report suggests that patients who are being treated with thalidomide and corticosteroids concomitantly for type 2 lepra reaction may be at risk of DVT, and suggests a possible mechanism for the thrombosis. Such patients should be monitored.

References